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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/548,748	09/08/2005	Markus Frank	12810-00137-US	1250

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EXAMINER	
IBRAHIM, MEDINA AHMED	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
07/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/548,748	FRANK ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7-9,11,14,16,17,19,20,23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7-9,11,14,16,17,19,20,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/08/09 has been entered.

Claims 1, 3, 7-9, 11, 14, 16-17, 19-20, 23 and 25 are pending and are examined.

All previous objections and rejections not set forth below have been withdrawn in view of Applicant's amendment to the claims and/or upon further consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3, 7-9, 11, 14, 16-17, 19-20, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simmons et al (WO 2002101079A2, Applicant's IDS) in view of Huckelhoven et al (Plant Mol. Biol. (2001) 47 (6):739-748), Sonnewald et al (US 6,229,067 B1), and Nelson et al (Ann. Phytopath. Soc. Japan (1989)55:156-160).

Simmons et al teach a method of increasing resistance to pathogens in a plant by transforming a plant a recombinant expression cassette comprising a nucleic acid encoding a Bax inhibitor I protein having at least 85% sequence identity to SEQ ID NO: 2 (see attached alignment of sequences) under the control of a tissue-specific promoter (pages 7-8; 19-20; see page 8, paragraph # 0117). The cited reference also teaches various methods of transforming a plant cell, selecting transformed cells, and

regenerating a stably transformed plant from the plant cell; plants to be transformed include monocots and dicots such maize, soybean, tobacco, potato, tomato, sunflower, canola, wheat, rice, and barley (pages 35-40; and Examples 5-12 and 14-15). Pathogens include fungal pathogens such as Altemaria, Botrytis, Erysiphe, Rhizopus oryzae, Rhizopus, Puccinia helianthi, Verticillium, Erwinia, Cephalosporium, Phytophthora and Fusarium (pages 44-46). The cited further teaches that either heterologous or non-heterologous promoters can be used with BI1 nucleic acids in expression cassettes to drive expression of antisense nucleic acids to reduce, increase, or alter concentration of the BI1 proteins in a desired tissue (page 20, lines 17-22). The mlo resistant phenotype or the inhibited expression or function of MLO, RacB and/or NaOx in the epidermis, or the increased expression of PEN2, SNAP34 and/or PEN1 would be an inherent property of transgenic plants expressing barley BaxI1 in the mesophyll cells.

While Simmons et al teach transformation and expression of a nucleic acid encoding a BaXI1 protein having more than 85% sequence identity to Applicant's SEQ ID NO: 2 in transgenic plant under a tissue-specific promoters, Simmons et al do not explicitly teach a nucleic acid encoding Applicant's SEQ ID NO: 2 and a mesophyll-specific promoter.

Huchelhoven et al teach a nucleic acid encoding a BaxI1 protein that is 100% identical to SEQ ID NO: 2 (alignment of sequences provided in the last Office action), its role in barley defense against *Bgh*, its functional relationship with the barley mlo resistant gene, and suggest the barley Bax inhibitor may have role in restricting the

spread of cell death in HR tissues after fungal attack. The cited reference further suggests tissue-specific expression of the Bax I1 in barley cells inoculated with Bgh be carried out (see the whole document).

Sonnewald et al teach mesophyll-specific promoters which can be used for the expression of any heterologous structural DNA. Sonnewald et al also teach a recombinant vector comprising a mesophyll-specific promoter that controls the expression of a desired gene such as a disease resistant gene in a transgenic plant or a microorganism comprising said recombinant vector (see at least the claims). At column 4, lines 49-56, Sonnewald et al state that the primary site of a large number of plant pathogens is the leaf tissue and suggest leaf-specific expression of a disease resistant gene using their promoter.

Nelson et al teach leaf mesophyll cells of barley are more susceptible to powdery mildew infection than epidermis cells and therefore; Nelson et al suggest a supportive role in defense mechanism by mesophyll cells (see at least the Abstract on page 156 and discussion on pages 157-158).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of transforming a plant with a nucleic acid encoding a BaxI1 inhibitor under the control of a tissue-specific promoter to induce resistance against a plant pathogen as taught by Simmons et al, and to modify that method by incorporating any other known BaxI1 nucleic acid such as the barley BaxI1 nucleic acid taught by Huchelhoven et al with any other known tissue-specific promoter such as the mesophyll-specific promoter taught by Sonnewald et al, with a reasonable

expectation of success as taught by Simmons et al. One would have been motivated to use the barley BaxI1 sequence, given that it is well characterized in its ability to induce defense reaction in tissue-specific manner as taught by Huchelhoven et al, and given the problem of plant pathogens in crop production as taught by Simmons et al. One would also have been motivated to use a mesophyll-specific promoter with BaxI1 gene given that the powdery mildew infection occurs more in the mesophyll rather than in other parts of the leaf such as the epidermis as taught by Nelson et al. One of ordinary skill in the art would expect that expression of the barley BaxI1 nucleic acid in a transgenic plant would induce resistance against any plant fungal pathogen as taught by Huchelhoven et al. Therefore, the claimed invention as whole was clearly a *prima facie* obvious.

Response to Arguments

Applicant argues that the difference between the prior art and the instant claims lies the use of a mesophyll-specific promoter to control the expression of a BI1 gene in a transgenic plant, and that none of the cited references teach or suggest the use of mesophyll-specific promoter. Applicant also argues that before the instant invention, it was not known in the prior art that fungal attack in plants occurs through different routes and Applicant asserts that none of the cited reference suggested a fungal attack through mesophyll cells which are interior layer below the leaf epidermis. Applicant, therefore, contends that the Office action fails to establish a prima facie case of

obviousness. Applicant cites MPEP 2141.02 and In re Sponnoble, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969) to support this position (response, pp. 6-8).

These arguments have been considered but are not deemed persuasive for the following reasons: firstly, the use of a mesophyll-specific promoter to express a desired gene such as a disease resistant gene is neither novel nor unobvious as evidenced by Sonnewald et al. Sonnewald et al teach the use of a mesophyll-specific promoter to control the expression of a desired gene. At column 4, lines 49-56, Sonnewald et al teaches that the primary site of a large number of plant pathogens is the leaf tissue and Sonnewald suggests leaf-specific expression of a disease resistant gene in transgenic plant may improve plant disease resistance. Secondly, Nelson et al, cited above, provide analysis of the respective roles of epidermis and mesophyll cells in the resistance of barley to Powdery mildew infection and discovered a possibility that mesophyll cells promote powdery mildew infection. Thirdly, at the time this application was filed one of skill in the art was able to select a suitable promoter for the expression of any desired gene in a desired plant tissue without any unexpected results. Applicant has not provided clear and convincing evidence to the contrary. In Example 7, Simmons et al teach methods of altering BI1 expression in transgenic plants using tissue-specific promoters. In Example 11 , the cited reference teaches methods of inducing resistance against ear mold disease by altering expression of the BI1 gene using promoters specific to the tissue most accounting for ear mold ingress, namely silks, husks, pericarp or cob to retard cell death and senescence. Example 13 of the specification

shows reducing the level maize BI1 in tapetum tissues using antisense BI1 constructs containing tapetum -specific promoter. .

Finally, one of ordinary skill in the art at the time this application was filed would be able to make a recombinant expression vector comprising any known BI1 gene such as the BI1 gene taught by Huchelhoven et al, with any suitable tissue specific promoter (the tissue most accounting for the pathogen to control) such as the mesophyll-specific promoter taught by Sonnewald et al to transform plants including monocot and dicot plants to produce transgenic plants having resistance to a pathogen as taught by Simmons et al. One would have been motivated to use a BI1 gene with a tissue-specific promoter, given the importance and availability of well characterized BI1 genes and mesophyll-specific promoters. In addition, since the rejection is one of obviousness and not one of anticipation, none of the cited references need teach BI1 gene is unchanged or reduced in leaf epidermis or teach the use of a mesophyll-specific promoter with the BI1 gene to transform a plant.

Regarding MPEP 2142.02 and the cited case law of in re Sponnoble, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969), it is noted that while the discovery of the disease resistance activity against powdery mildew without breaking the mlo resistance phenotype is not mentioned in the prior art, this property is considered an inherent property of the transgenic plants expressing BaxI1 protein is tissue-specific manner as suggested by Huchelhoven et al. Huchelhoven et al teach expression pattern of other defense-related genes with the barley PCD gene, in this case the barley BaxI1 gene.

Also, Nelson et al above teach that leaf mesophyll cells of barley provide favorable environment for powdery mildew infection. Huchelhoven et al above teach that expression of BaxI1 protein was enhanced after inoculation of powdery mildew. Therefore, one of skill in the art would have been motivated to use mesophyll-specific cells when combating powdery mildew infection which is common disease in barley plants to produce transgenic plants having increased disease resistance. Therefore, neither the MPEP 2142 nor the cited case law supports Applicants' position. The MPEP 2142 also states that simple substitution of known element for another yields predictable results to one of ordinary skill in the art. See KSR International Co. v. Teleflex Inc. (KSR), 550 U.S. ___, 82 USPQ2d 1385 (2007) cited in the last Office action.

See also United States v. Adams, . . . [t]he Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result." Id. at ___, 82 USPQ2d at 1395"; *Ex parte Kubin, 83 USPQ2d 1410 (Bd. Pat. App. & Int.2007)*.

Remarks

1. No claim is allowed

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is

(571)272-0797. The examiner can normally be reached on M-TH 8:00 am to 5:30 PM, and every other Friday from 8:00 AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MAI /Medina A Ibrahim/

7/14/2009 Primary Examiner, Art Unit 1638